

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES
PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro



(43) Internationales Veröffentlichungsdatum
22. Januar 2004 (22.01.2004)

PCT

(10) Internationale Veröffentlichungsnummer
WO 2004/007523 A1

- (51) Internationale Patentklassifikation⁷: **C07J 73/00**
- (21) Internationales Aktenzeichen: PCT/CH2003/000435
- (22) Internationales Anmeldedatum:
2. Juli 2003 (02.07.2003)
- (25) Einreichungssprache: Deutsch
- (26) Veröffentlichungssprache: Deutsch
- (30) Angaben zur Priorität:
1242/02 16. Juli 2002 (16.07.2002) CH
1375/02 8. August 2002 (08.08.2002) CH
0015/03 8. Januar 2003 (08.01.2003) CH
- (71) Anmelder (für alle Bestimmungsstaaten mit Ausnahme von
US): SIEGFRIED LTD. [CH/CH]; Untere Brühlstrasse 4,
CH-4800 Zofingen (CH).
- (72) Erfinder; und
- (75) Erfinder/Anmelder (nur für US): SCHÄRER, Norbert
[CH/CH]; Rütliweg 8, CH-5036 Oberentfelden AG (CH).
WEBER, Beat [CH/CH]; Wiesenstrasse 4, CH-4800
Zofingen (CH). MÜLLER, Beat, W. [CH/CH]; Vogesen-
strasse 31, CH-4106 Therwil/BL (CH).
- (74) Anwalt: BRAUN, André; Braun & Partner, Reusstrasse
22, CH-4054 Basel (CH).

(81) Bestimmungsstaaten (national): AE, AG, AL, AM, AT
(Gebrauchsmuster), AT, AU, AZ, BA, BB, BG, BR, BY,
BZ, CA, CH, CN, CO, CR, CU, CZ (Gebrauchsmuster),
CZ, DE (Gebrauchsmuster), DE, DK (Gebrauchsmuster),
DK, DM, DZ, EC, EE (Gebrauchsmuster), EE, ES, FI (Ge-
brauchsmuster), FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK
(Gebrauchsmuster), SK, SL, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Bestimmungsstaaten (regional): ARIPO-Patent (GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ,
TM), europäisches Patent (AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL,
PT, RO, SE, SI, SK, TR), OAPI-Patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

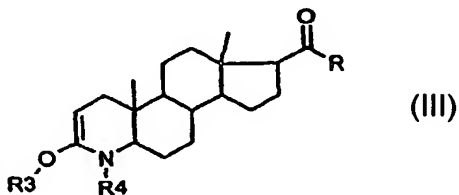
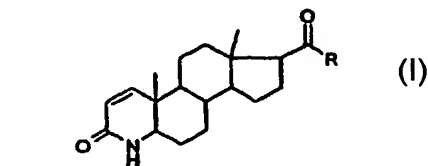
Veröffentlicht:

— mit internationalem Recherchenbericht

Zur Erklärung der Zweibuchstaben-Codes und der anderen Ab-
kürzungen wird auf die Erklärungen ("Guidance Notes on Co-
des and Abbreviations") am Anfang jeder regulären Ausgabe der
PCT-Gazette verwiesen.

(54) Title: METHOD FOR INTRODUCING A 1,2 DOUBLE BOND INTO 3-OXO-4-AZASTEROID COMPOUNDS

(54) Bezeichnung: VERFAHREN ZUR EINFÜHRUNG EINER 1,2-DOPPELBINDUNG BEI 3-OXO-4-AZASTEROIDVERBIN-
DUNGEN



(57) **Abstract:** The invention relates to a method for producing 17 β -substituted 4-aza-androst-1-ene-3-one compounds of the general formula (I), or a pharmaceutically approved salt thereof by (A) introducing protective groups into the 3-keto-4-aza group of the corresponding 1,2-dihydro compound, thereby producing a compound of the general formula (III), (B) reacting the compound so obtained in the presence (i) of a dehydration catalyst, and in the presence of (ii) optionally substituted benzoquinone, allylethylcarbonate and/or allylpropylcarbonate, and, (C) removing the protective groups R₃ and R₄ and optionally converting the compound so obtained to a salt.

(57) **Zusammenfassung:** Verfahren zur Herstellung von 17 β -substituierten 4-Aza-androst-1-en-3-on-Verbindungen der allgemeinen Formel (I), oder einem pharmazeutisch zugelassenen Salz derselben, indem man (A) in die 3-Keto-4-aza-Gruppierung der entsprechenden 1,2-Dihydroverbindung Schutzgruppen einführt, so dass eine Verbindung der allgemeinen Formel (III) entsteht; (B) die erhaltene Verbindung in Gegenwart (i) eines Dehydrierungskatalysators, und in Gegenwart von (ii) gegebenenfalls substituiertem Benzochinon, Allylpropylcarbonat, umsetzt; und, (C) die Schutzgruppen R₃ und R₄ entfernt und gegebenenfalls die erhaltene Verbindung in ein Salz umwandelt.

und in Gegenwart von (ii) gegebenenfalls substituiertem Benzochinon, Allylpropylcarbonat, umsetzt; und, (C) die Schutzgruppen R₃ und R₄ entfernt und gegebenenfalls die erhaltene Verbindung in ein Salz umwandelt.

WO 2004/007523 A1

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CH 03/00435

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07J73/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 298 652 A (MERCK & CO INC) 11 January 1989 (1989-01-11) examples 1-9, 12-37	1-21
Y	EP 0 428 366 A (MERCK & CO INC) 22 May 1991 (1991-05-22) example 1	1-21
	--- -/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

24 September 2003

Date of mailing of the international search report

08/10/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Watchorn, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CH 03/00435

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	RASMUSSEN G H ET AL: "AZASTEROIDS: STRUCTURE-ACTIVITY RELATIONSHIPS FOR INHIBITION OF 5ALPHA-REDUCTASE AND OF ANDROGEN RECEPTOR BINDING" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 29, no. 11, 1 November 1986 (1986-11-01), pages 2298-2315, XP000568779 ISSN: 0022-2623 page 2309, column 1, paragraph 4	1-21
Y	BHATTACHARYA APURBA ET AL: "Silylation-mediated oxidation of 4-aza-3-ketosteroids with DDQ proceeds via DDQ-substrate adducts" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 110, 1988, pages 3318-3319, XP002179347 ISSN: 0002-7863 page 3319, column 1; figure 1 page 3319, column 2, paragraph 2	1-21
Y	US 5 710 342 A (IMRE LASZLO ET AL) 20 January 1998 (1998-01-20) column 4, line 2	1-21
Y	J. TSUJI ET AL: "PALLADIUM CATALYZED PREPARATION OF 1alpha-ALLYL ETHERS AND alpha,beta-UNSATURATED ESTERS FROM SATURATED ESTERS VIA THEIR KETENE SILYL ACETALS" TETRAHEDRON LETTERS., vol. 25, no. 42, 1984, pages 4783-4786, XP002226639 ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM., NL ISSN: 0040-4039 cited in the application page 4783; figure 1 page 4785, paragraph 1	1-21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CH 03/00435

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0298652	A	11-01-1989	AT 117317 T	15-02-1995
			AU 608860 B2	18-04-1991
			AU 1845788 A	05-01-1989
			CA 1331601 C	23-08-1994
			CY 1871 A	05-04-1996
			DE 3852790 D1	02-03-1995
			DE 3852790 T2	17-08-1995
			DK 58098 A	28-04-1998
			DK 355088 A	24-02-1989
			EP 0298652 A2	11-01-1989
			ES 2066786 T3	16-03-1995
			GR 3015690 T3	31-07-1995
			HK 116695 A	21-07-1995
			IE 64996 B1	04-10-1995
			IL 86821 A	13-05-1993
			JP 1079198 A	24-03-1989
			JP 1992450 C	22-11-1995
			JP 7025791 B	22-03-1995
			KR 9615038 B1	24-10-1996
			NZ 225100 A	25-09-1991
			PT 87777 A , B	31-05-1989
			ZA 8804610 A	22-02-1989
EP 0428366	A	22-05-1991	US 5021575 A	04-06-1991
			CA 2029859 A1	14-05-1991
			CY 2079 A	16-10-1998
			DE 69022540 D1	26-10-1995
			DE 69022540 T2	02-05-1996
			DE 69033538 D1	08-06-2000
			DE 69033538 T2	04-01-2001
			EP 0428366 A2	22-05-1991
			EP 0655459 A2	31-05-1995
			HK 1002708 A1	11-09-1998
			JP 1924484 C	25-04-1995
			JP 3206096 A	09-09-1991
			JP 6051718 B	06-07-1994
			LV 12572 A	20-11-2000
			LV 12572 B	20-04-2001
US 5710342	A	20-01-1998	DE 4444738 A1	20-06-1996
			EP 0717025 A2	19-06-1996
			JP 8259491 A	08-10-1996